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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/812,382	03/20/2001	Ashutosh Chilkoti	4176-101	1286

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EXAMINER

WALICKA, MALGORZATA A

ART UNIT PAPER NUMBER

1652

DATE MAILED: 02/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/812,382

Applicant(s)

CHILKOTI, ASHUTOSH

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 December 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-10,12-19,21-28,31,32,62-72 and 74-77 is/are pending in the application.

4a) Of the above claim(s) 62-65 is/are withdrawn from consideration.

- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-10,12-19,21-28,31,32,71,72 and 74-77 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

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The Amendment of Dec. 4, 2002, filed as paper No. 11 and Drawings filed on Dec. 17, 2002 are acknowledged. Amendments to the claims have been entered as requested. Claims 1, 8, 12, 21, 25-27, 31, 71 and 74 are amended. Claims 2, 11, 20, 29, 30, 33-61, and 73 are cancelled. Claims 1, 3-10, 12-19, 21-28, 31-32, 62-72 and 74-77 are pending. Claims 1, 3-10, 12-19, 21-28, 31- 32 and 66-77 are the subject of this Office Action. Claims 62-65 are withdrawn from consideration as directed to non-elected invention.

DETAILED ACTION

1. Election/Restriction

Applicant's request for rejoinder of Group III, claim 62 and Group IV, claims 63-65 is acknowledged. Upon finding claim(s) of Group I directed to an allowable product, pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86), claim 62 and 63-65, directed to the processess of using the patentable product, previously withdrawn from consideration as a result of a restriction requirement, will be rejoined and fully examined for patentability under 37 CFR 1.104.

2. Objections

2.1. Drawings

The drawings filed on December 27, 2007 are accepted with exception of Fig. 3 that is still objected to for the wrong spelling of the name tendamistat.

2.2. Claims

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Objections to claims 71-75 are withdrawn because Claim 71 has been amended.

Objection to claim 29 is withdrawn because the claim has been cancelled

3. Rejections

3.1. 35 USC section 112, second paragraph

Claim 1-8, 20, 25-26, 31 and 33 were rejected in the previous Office Action, paper No. 10, under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection of claims 1-7, 20, 25-26, 31 and 33 is withdrawn in the light of the amendments. However, the amended claims 1-7, 20, 25-26, 31 and 33 are rejected because they recite as part (b) "one or more phase transition proteins that exhibit an inverse phase transition". This recitation is confusing. The fusion proteins disclosed comprise as part (b) a pentapeptide or its oligomeric repeats, up to 90 times. Therefore, at least when the repeats are in the range 1-20 part (b) consists of peptides of 5-100 amino acids. Thus, part (b) as disclosed in the specification comprises a peptide or a protein depending on the number of involved repeats of the basic pentapeptide. For examination purposes it is assumed that part (b) is directed to peptides or proteins.

The amended claim 8, being dependent on claim 7 recites the limitation "biological molecule of interest " in the second line. There is insufficient antecedent basis for this limitation in the claim, because claim 7 does not recite "biological molecule

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of interest.” It is suggested that claim 8 be depended only on claim 1 and recited: “biological molecule of claim 1(a)”.

Claim 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims contain the abbreviation ELP, which should be expanded when used for the first time. In addition, the claims are confusing. The term ELP is used in claims in two meanings. Firstly, the term ELP is used to mean “elastin-like peptide” which is the pentapeptide Val-Pro-Gly-X-Gly. Secondly, the term ELP is used to mean the whole elastin –like peptide fusion protein, which consists in 75%, 85% or 95% of the elasin-like peptide residues.

Claim 71 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim recites the term “composition conditions”, and the phrase “predetermined change of composition conditions”. Neither the claim nor the specification define the term “composition conditions” and the phrase “predetermined change of composition conditions.” Thus, the term and phrase are indefinite and render the claim indefinite.

Claim 72 being dependent on claim 71 recites the limitation “comprising a protein of interest cleavable from the ELP at a cleavage site of the ELP fusion protein”. There is insufficient antecedent basis for this limitation in the claim, because claim 71 does not recite any protein of interest or a cleavage site.

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Claim 76 is rejected because the claim does not further limit the claim from which it depends. Claim 76 recites the phase transition protein(s) comprising a β -turn structure. Claim 76 depends on claim 12 that recites the phase transition proteins(s) comprising oligomeric repeats of pentapeptide Val-Pro-Gly-X-Gly. By definition, page 13, line 15 of the specification, these oligomeric repeats comprise a β -turn structure.

Claim 77 is rejected as dependent on the cancelled claim 35.

3.2. 35 USC section 112, first paragraph

3.2.1. Lack of written description

Claim 22-24 were rejected in the previous Office Action, paper No.10. The rejection is withdrawn because the Applicants' arguments regarding signaling peptides have been found persuasive.

Rejection of Claim 26 is withdrawn, because the claim has been amended.

Claims 1, 3-10, 12, 13-19, 27-28, 31-32 and 76 are rejected under 35 U.S.C. 112, first paragraph for the reasons stated in the previous Office Action, paper No. 10, and reiterated below.

The claims are directed to a fusion protein exhibiting a phase transition, comprising one or more peptides or proteins (a), one or more proteins exhibiting inverse phase transition (b) and a spacer (c). Thus, the claims are directed to large and variable genus of fusion proteins exhibiting a phase transition. However, neither the claim nor the specification set forth the limitation for structure of proteins of part (a), and

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neither the claims nor the specification do particularly point out which features of said proteins ensure the capacity of exhibiting the phase transition of the fused protein the part of which said proteins are going to be. The specification teaches two species of the genus, thioredoxin and tendamistat, small molecules containing 108 and 74 amino acids. This is not sufficient for identifying the features of all proteins that are able to support the capacity of exhibiting the phase transition.

In their response, page 7, line 26 Applicants state, "The ELP tag can be attached to **any peptide or protein** [emphasis added] of interest to form the ELP-tagged fusion protein of the present invention wherein the ELP-tagged fusion protein exhibits an inverse phase transition."

Applicants' argument has been fully considered but is found not persuasive. For example, it is doubtful that large proteins, with molecular weight higher than 100,000 Da, exhibiting a large positive charge, are good candidates for part (a) of the claimed fusion protein.

Claims 1, 3-10, 27-28, and 31-32 are also rejected because they do not set forth the sequences of the phase transition protein (b) that are to be used for constructing the fusion protein. The genus of the phase transition proteins known to those skilled in the art is a large genus. The applicants disclose the fusion proteins in which part (b) is a peptide or protein comprising up to 90 units of pentapeptides Val-Pro-Gly-X-Gly. This pentapeptide or a peptide or a protein consisting of it is not a species that represents the structure of all elastin-like polypeptides.

Taking into account lack of written description of structures of the species of the genus of proteins of part (a) and (b) it is concludes that the inventors were not in possession of the claimed invention at the time the application was filed.

Claims 71–72 and 74-75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 71–72 and 74-76 are directed to a large and variable genus of compositions comprising fusion proteins for which the specification fails to give sufficient structural description. The specification sets forth only the following fusion proteins:

- 1) the fusion proteins consisting of thioredoxin, protease cleavable spacer and up to 90 repeats of the pentapeptide Val-Pro-Gly-X-Gly,
- 2) the fusion proteins consisting of tendamistat, protease cleavable spacer and up to 90 repeats of the pentapeptide Val-Pro-Gly-X-Gly, and
- 3) the fusion proteins consisting of thioredoxin, protease cleavable spacer and up to 90 repeats of the pentapeptide Val-Pro-Gly-X-Gly and tendamistat,

wherein the spacer is cleavable by thrombin.

Description of these three types of fusion proteins is insufficient to identify all elastine-like fusion proteins as encompass by the scope of claim 71 and dependent claims. Applicants did not provide sufficient identifying characteristics of the claimed

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invention so that one skilled in the art was convinced that at the time the application was filed, Applicants had possession of the claimed invention.

Taking into account lack of written description of structures of the species of the genus of fusion proteins it is concluded that the inventors were not in possession of the claimed invention at the time the application was filed.

Claim 9 and 66-70 are rejected because neither the claim nor the specification describe the phase transition of the claimed fusion protein wherein the phase transition is mediated by changing pH, addition of solutes and/or solvents, side chain ionization, chemical modification, and changing pressure. The disclosure set forth the phase transition induced by changes of the temperature, when other conditions are constant. Therefore, because claims 66-70 are lacking written description changing pH, addition of solutes and/or solvents, side chain ionization, chemical modification, and changing pressure, one skilled in the art is not convinced the inventors were not in possession of the claimed invention at the time the application was filed.

3.2.2. Scope of enablement

Rejection of claim 1, 3-10, 2-19, 21-28, 31-32, 66-72 and 74-75 under 35 U.S.C. 112, first paragraph, made in the previous Office Action, paper No. 10 is withdrawn in the light of Applicants' arguments.

3.3. 35 USC, section 102

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Rejection of claim 71 made under this paragraph in the previous Office Action, paper No.10, is withdrawn, because the claim has been amended.

However, claims 1, 4, 6, 21, 25, 26, 27, 28, 31 are rejected under 35 U.S.C. 102(b) as being anticipated by McPherson et al. (Production and Purification of a Recombinant Elastomeric Polypeptide, G-(VPGVG)₁₉-VPGV, from *Escherichia coli*, Biotechnol. Prog. (1992), 8, 347-352, enclosed in Information Disclosure Statement).

The claims are directed to a fusion protein exhibiting a phase transition, the fusion protein comprising: (a) one or more biological molecules selected from the group consisting of peptides and proteins: (b) one or more phase transition peptides or proteins that exhibit an inverse phase transition and optionally, a spacer sequence (c) separating part (b) from part (a), wherein part (a) comprises:

a protein,

a biologically active protein or

an enzyme useful in industrial biocatalysis, and

wherein part b) comprises

a peptide,

a protein or

a pentapeptide Val-PRO-GLY-X-Gly and

wherein the spacer is a peptide or a protein and wherein the spacer comprises a proteolytic cleavage site, and wherein the fusion protein is recombinantly produced.

McPherson et al. teach a fusion protein consisting of glutathione S-transferase joined through glycine spacer to the pentapeptide (VPGVG)₁₀ or to (VPGVG)₁₉ – VPGV.

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The glycine spacer creates a protease recognition site for protease factor Xa (page 347, abstract, and the right column above "Materials and Methods" of the article). The protein disclosed by McPherson consists of a fusion of glutathione S-transferase and one or repeats of pentapeptide Val-Pro-Gly-X-Gly wherein X is a valine. Glutathione S-transferase is a biologically active protein and an enzyme having industrial application. McPherson and colleagues produced their fusion protein by expressing the encoding DNA molecule in E. coli. McPherson and co-workers teach the fusion protein having characteristics of that claimed by Applicants in claims 1, 4, 6, 21, 25, 26, 27, 28, 31.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.


If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

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Patent Examiner



PONNATHAPURA ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNICAL STAFF